tissue products and how this applies to cord blood units. She indicated that peripheral blood stem cells and cord blood are regulated as biologic cell therapies under the tissue approach. Implementation of the regulatory approach is under way, and a period of enforcement discretion for unrelated donor cord blood is ongoing. Cord blood manufacturers currently must register with the Food and Drug Administration. Finalizing regulations is currently a Food and Drug Administration priority. There is a recognized need for international harmonization of cord blood regulations.

Symposium Abstracts

1

CORD BLOOD TRANSPLANTATION TO ADULT PATIENTS: A SINGLE-BANK'S EXPERIENCE

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Since 1993, the New York Blood Center has provided cord blood (CB) grafts to more than 1500 recipients, 421 of whom where adults (age ≥16). These patients were treated in 53 US and 26 non-US Transplant Centers (TCs). Data from 391 (92.9%) are available. The proportion of adult recipients has grown from 9% in 1995 to over 30% in 2001-2003. More than 90% (363/391) had leukemia (41% advanced), lymphoma, or myelodysplasia. No. of patients aged 16-24, 25-39, and >40: 130, 135, and 125, respectively; there were 15% African American recipients, 13.3% Hispanic, and 65.6% Caucasoids, respectively. TNC doses $<2.5 \times 10^7$/kg were given to 62%, 25-49 $\times 10^7$/kg to 37%, and $>5 \times 10^7$/kg to 1.3% of all recipients. HLA was matched at serological levels for A and B and at DNA allele level for HLA-DR. Seven TCs have performed ≥10 CB transplantations each. Neutrophil engraftment was significantly reduced when TNC doses $<2.5 \times 10^7$/kg and stratified significantly with HLA mismatch levels. Engraftment was superior with TBI conditioning compared to no TBI; and regimens including methotrexate associated with reduced engraftment. Overall survival was 30.2% at one year and 23% at five years post-transplant. Centers with ≥10 CB transplantations had better survival (by Cox Regression analysis) and so did those with better HLA matches, those without advanced stage leukemia, and those whose conditioning included fludarabine. The effect of cell dose was not significant in the Cox regression. Patients with good HLA matches (6/6 and 5/6 without rejection mismatches) and those conditioned with regimens including TBI and fludarabine had excellent survival: 68% at one year, respectively.

The data indicate that, despite the low graft cell doses, remarkable improvement in overall survival rate of adults transplanted with cord blood is possible by improvements in HLA matching and conditioning regimens.

2

UMBILICAL CORD BLOOD TRANSPLANTATION: NOVEL APPROACHES TOWARD IMPROVING ENGRAFTMENT

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Cryopreserved umbilical cord blood (UCB) has been investigated as a potential strategy for augmenting the pool of acceptable donors, reducing the risks of acute and chronic graft-versus-host disease (GVHD) and improving survival. Cell dose, however, has clearly been identified as a major limitation, often preventing the consideration of UCB for adult recipients. Recipients of $<1.7 \times 10^5$CD34/kg have slow hematopoietic recovery (median 35 days) and significantly lower incidence of engraftment (68% [95% CI, 46-91]). Therefore, strategies for increasing the cell dose, e.g., *ex vivo* HSC expansion, transplantation of multiple UCB units, and co-infusion of healthy haploidentical mesenchymal stem cells (MSC), are being explored.

Multi-unit UCB transplantation. Twenty-three adult and adolescent patients [median age 24 years (range: 13-53)] with high-risk hematologic malignancy were transplanted with two partially HLA-matched UCB units after myeloablative conditioning. The median total infused dose 3.5×10^7NC/kg (range 1.1-6.3). All evaluable patients (n = 21) engrafted at a median of 23 days (range 15-41) with one unit predominating. While there was no association between nucleated cell dose, CD34+ cell dose, or HLA-A,B,DRB1 match and which unit predominated, the winning unit had a higher CD3+ dose. Incidence of severe III-IV acute graft-versus-host disease (GVHD) was 13% (0-26%), and disease-free survival was 57% (95% CI: 35-79) at 1 year. These data suggest that 1) double unit UCBT is safe with one unit predominating over time, 2) the unit that disappears over time may facilitate engraftment of the winning unit, possibly by immune mediated mechanisms, and 3) CD3 dose might predict which unit will ultimately engraft long term. Most importantly, the use of two UCB units extends the application of this treatment to nearly all adults for whom one unit would have been insufficient.

Co-Infusion of haploidentical MSC and UCB transplantation. Fifteen patients [median age 7.5 years (range: 0.2-16)] with high risk leukemia were transplanted with HLA 0-2 antigen mismatched UCB and haploidentical parental donor MSC after a myeloablative conditioning. No toxicity was observed related to the infusion of MSC. All treated patients (n = 8) had hematopoietic recovery and complete chimerism at a median of 19 days (range: 9-28). Platelet recovery occurred at a median of 1.7 months (range: 1.2-3.3). Incidence of grade II-IV acute GVHD was 2 of 8 patients with no patient having chronic disease. With a median followup of 2.9 years, 6 patients are alive and disease free with two patients dying of infections on days 53 and 63, respectively. These data suggest that engraftment, particularly platelet recovery, may be enhanced by the co-infusion of MSC. Clearly larger patient numbers are required to confirm these preliminary observations.

3

UMBILICAL CORD BLOOD TRANSPLANTATION AFTER A NON-MYELOABLATIVE THERAPY IN HIGH RISK ADULTS

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Bone marrow transplantation (BMT) in adults is associated with a high risk of graft-versus-host disease (GVHD), opportunistic infection and regimen related toxicity. For these reasons, umbilical cord blood (UCB) after a non myeloablative preparative regimen has been explored.

Fifty-one adults with advanced hematologic malignancies [median age 50 years (range 19-60)], ineligible for myeloablative conditioning by virtue of advanced age, extensive prior therapy or serious co-morbidities received UCB transplantation after cyclophosphamide 50 mg/kg, fludarabine 200 mg/m^2, and 200 cGy TBI. Immunosuppression was with cyclosporine-A to at least day 100 and mycophenolate mofetil to day 30. Eight patients with no combination chemotherapy in the 6 months prior to transplant also received ATG during conditioning. Thirteen patients (25%) received single UCB units and 38 (75%) received double unit grafts. The median total infused cell dose was 3.4×10^7NC/kg (range 1.1-5.7). Units were predominantly 1-2 antigen HLA mismatched with the recipient. Of 50 evaluable patients, neutrophil recovery occurred at a median of 8 days (range 5-32). Four patients had failure of donor derived engraftment with autologous recovery and 1 had late graft rejection. The cumulative incidence of sustained donor engraftment